Amendments to the Claims

Claims 1-104. (Cancelled).

105. (New) A butyrylcholinesterase variant comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 4, 6, 8, 10, 12, 14, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, and 196, or a functional fragment thereof, wherein the variant or fragment comprises alanine at amino acid position 227.

106. (New) The butyrylcholinesterase variant of Claim 105, wherein the amino acid sequence is selected from the group consisting of SEQ ID NO: 24, 26, 30, 32, 34, 36, 38, 104, 106, 108, 110, 112, 116, 118, 120, 122, 124, 126, 128, 132, 134, 136, 140, and 142, or a functional fragment thereof.

107. (New) The butyrylcholinesterase variant of Claim 106, wherein the amino acid sequence is selected from the group consisting of SEQ ID NO: 36, 108, 110, 112, 122, 124, 134, 178, 180, 182, 186, 188, 190, 192 and 196, or a functional fragment thereof.

108. (New) The butyrylcholinesterase variant of Claim 107, wherein the amino acid sequence is selected from the group consisting of SEQ ID NO: 178, 180, and 188, or a functional fragment thereof.

109. (New) The butyrylcholinesterase variant of Claim 108, wherein the amino acid sequence is SEQ ID NO: 180 or a functional fragment thereof.

110. (New) The butyrylcholinesterase variant of Claim 105, having at least a two-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

111. (New) The butyrylcholinesterase variant of Claim 110, having at least a fifty-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

112. (New) The butyrylcholinesterase variant of Claim 111, having at least a one hundred-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

113. (New) The butyrylcholinesterase variant of Claim 112, having at least a five hundred-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

114. (New) The butyrylcholinesterase variant of Claim 113, having at least a fifteen hundred-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

115. (New) The butyrylcholinesterase variant of Claim 114, having at least a two thousand-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

116. (New) The butyrylcholinesterase variant of Claim 115, having at least a two thousand five hundred-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

117. (New) The butyrylcholinesterase variant of Claim 116, having at least a three thousand-fold increase in camptothecin conversion activity compared to butyrylcholinesterase, or functional fragment thereof.

118. (New) The butyrylcholinesterase variant of Claim 105, or functional fragment thereof, further comprising an antibody or antibody fragment which specifically binds the epidermal growth factor receptor (EGFR).

119. (New) The butyrylcholinesterase variant of Claim 118, wherein the antibody or antibody fragment comprises an amino acid sequence as shown in SEQ ID NO: 18 or 20.

120. (New) The butyrylcholinesterase variant of Claim 105, further comprising an antibody or antibody fragment which specifically binds the CD20 cell surface antigen.

121. (New) The butyrylcholinesterase variant of Claim 120, wherein the antibody or antibody fragment comprises an amino acid sequence as shown in SEQ ID NO: 198.

122. (New) A nucleic acid encoding a butyrylcholinesterase variant comprising the nucleic acid sequence selected from the group consisting of SEQ ID NO: 3, 5, 7, 9, 11, 13, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53 , 55, 57, 59, 61, 63, 65, 67, 69, 71,

73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, and 195, or a fragment thereof.

123. (New) The nucleic acid of Claim 122, wherein the nucleic acid sequence is selected from the group consisting of SEQ ID NO: 177, 179, 181, 183, 185, 187, 189, 191, 193, and 195, or a fragment thereof.

124. (New) A method of converting a camptothecin derivative to a topoisomerase inhibitor comprising contacting said camptothecin derivative with a butyrylcholinesterase variant comprising an amino acid sequence selected from SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140; 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194 and 196, or functional fragment thereof, under conditions that allow conversion of a camptothecin derivative to a topoisomerase inhibitor.

125. (New) The method of Claim 124, wherein said butyrylcholinesterase variant is selected from the group consisting of SEQ ID NOS: 24, 26, 30, 32, 34, 36, 38, 104, 106, 108, 110, 112, 116, 118, 120, 122, 124, 126, 128, 132, 134, 136, 140 and 142, or functional fragment thereof.

126. (New) The method of Claim 125, wherein said butyrylcholinesterase variant is selected from the group consisting of SEQ ID NO: 178, 180, 182, 184, 188 and 192, or functional fragment thereof.

127. (New) The method of Claim 126, wherein said butyrylcholinesterase variant is SEQ ID NO: 180, or functional fragment thereof.

128. (New) The method of Claim 124, wherein said butyrylcholinesterase variant exhibits a two-fold or greater increase in conversion capability compared to butyrylcholinesterase.

129. (New) The method of Claim 128, wherein said butyrylcholinesterase variant exhibits a fifty-fold or greater increase in conversion capability compared to butyrylcholinesterase.

130. (New) The method of Claim 129, wherein said butyrylcholinesterase variant exhibits a one hundred-fold or greater increase in conversion capability compared to butyrylcholinesterase.

131. (New) The method of Claim 130, wherein said butyrylcholinesterase variant exhibits a five hundred-fold or greater increase in conversion capability compared to butyrylcholinesterase.

132. (New) The method of Claim 131, wherein said butyrylcholinesterase variant exhibits a fifteen hundred-fold or greater increase in conversion capability compared to butyrylcholinesterase.

133. (New) The method of Claim 132, wherein said butyrylcholinesterase variant exhibits a two thousand-fold or greater increase in conversion capability compared to butyrylcholinesterase.

134. (New) The method of Claim 133, wherein said butyrylcholinesterase variant exhibits a two thousand five hundred-fold or greater increase in conversion capability compared to butyrylcholinesterase.

135. (New) The method of Claim 134, wherein said butyrylcholinesterase variant exhibits a three thousand-fold or greater increase in conversion capability compared to butyrylcholinesterase.

136. (New) The method of Claim 124, wherein said topoisomerase inhibitor is SN-38.

137. (New) The method of Claim 136, wherein said camptothecin derivative is CPT-11.

138. (New) A method of treating cancer comprising administering to an individual an effective amount of a butyrylcholinesterase variant selected from SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144,146, 148, 150, 152, 154, 156, 158, 160, 162, 164,166,168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, and 196, or functional fragment thereof, exhibiting increased capability to convert a camptothecin derivative to a topoisomerase inhibitor compared to butyrylcholinesterase.

139. (New) The method of Claim 138, wherein said cancer is metastatic colorectal cancer.

140. (New) The method of Claim 138, wherein said cancer is ovarian cancer.

141. (New) The method of Claim 138, wherein said cancer is lung cancer.

142. (New) The method of Claim 138, wherein said cancer is non-Hodgkin's lymphoma.

143. (New) The method of Claim 138, wherein said topoisomerase inhibitor is SN-38.

144. (New) The method of Claim 143, wherein said camptothecin derivative is CPT-11.

145. (New) The method of Claim 138, wherein said butyrylcholinesterase variant further comprises an antibody or antibody fragment that specifically binds the epidermal growth factor receptor (EGFR).

146. (New) The method of Claim 145, wherein said antibody or antibody fragment comprises an amino acid sequence as shown in SEQ ID NOS: 18 and 20.

147. (New) The method of Claim 138, wherein said butyrylcholinesterase variant further comprises an antibody or antibody fragment that specifically binds the CD20 cell surface antigen.

148. (New) The method of Claim 147, wherein said antibody or antibody fragment comprises an amino acid sequence as shown in SEQ ID NO: 198.

149. (New) The method of Claim 138, wherein said butyrylcholinesterase variant comprises the amino acid sequence designated as SEQ ID NO: 180, or functional fragment thereof.

150. (New) The method of Claim 138, wherein said functional fragment is an L530 truncation (SEQ ID NO: 201).